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EXAMINER

DELACROIX MUIRHEI, CYBILLE

ART UNIT	PAPER NUMBER
1614	//

DATE MAILED: 02/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/800,855	SONIS ET AL.
Examiner	Art Unit	
Cybille Delacroix-Muirh id	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 20 September 2001.

2a) This action is FINAL. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-27 is/are pending in the application.

4a) Of the above claim(s) 2,3,8-11 and 16-18 is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 1,4-7,12-15 and 19-27 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:

1. Certified copies of the priority documents have been received.

2. Certified copies of the priority documents have been received in Application No. _____.

3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4.

4) Interview Summary (PTO-413) Paper No(s). _____

5) Notice of Informal Patent Application (PTO-152)

6) Other: _____

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DETAILED ACTION

The following is responsive to Applicant's election received Sep. 20, 2001 and the interview summary of Feb. 5, 2002.

Applicant's election of Group I claims 1-27, with a further election of species to an MMP inhibitor (tetracycline) and an inflammatory cytokine inhibitor (IL-6 inhibitor) is acknowledged.

Non-elected claims 28-34 are cancelled.

Claims 2, 3, 8, 9, 10, 11, 16, 17, 18 are withdrawn from consideration.

No prior art was found for the IL-6 inhibitor. The search was expanded to another inflammatory cytokine inhibitor, pentoxifylline. Claims 1, 4-7, 12-15, 19-27 read on the elected species.

Information Disclosure Statement

Applicant's Information disclosure Statement received March 7, 2001 has been considered in part. The remaining references will be considered upon receipt of the parent application 09/265,299.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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2. Claims 15, 19 is rejected under 35 U.S.C. 102(b) as being anticipated by Schenk et al. (of record in parent application 09/265,299).

Schenk et al. disclose the invention substantially as claimed. Specifically, Schenk et al. teach topical formulations comprising tetracycline HCL in an amount effective to treat mucositis.

Please refer to the abstract; page 428, Treatment.

3. Claims 15, 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Rothwell et al. (of record in parent application 09/265,299).

Rothwell et al. disclose the invention substantially as claimed. Specifically, Rothwell et al. teach oral rinse compositions comprising tetracycline as well as other active agents. The oral rinse compositions are used in methods of treating mucositis in cancer patients undergoing radiation to the head and neck region. The patients were to rinse four times daily and continued through the treatment period. Please see the abstract; page 22, second and third column to the top of page 23.

Concerning the additional agents in the composition of Rothwell, Applicant's claims recite "comprising" language, which "opens claim[s] to other unspecified ingredients, even in major amounts." See Ex parte Davis, 80 USPQ 448.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

6. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schenk et al., supra or Rothwell et al, supra in view of Stogniew et al., 6,239,119.

Rothwell or Schenk as applied above.

Rothwell or Schenk do not specifically disclose treating mucositis with minocycline; however, the Examiner refers to Stogniew et al., which discloses methods for treating mucosal

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tissue damage (mucositis) associated with radiation and/or chemotherapeutic treatment of cancers, the method comprising administering amifostine as well as additional compounds, such as minocycline. Please see the abstract; col. 9, lines 42-56, especially line 56.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods of Schenk and Rothwell to administer minocycline because Stogniew suggest that minocycline may be useful in the treatment of mucositis and one of ordinary skill in the art would reasonably expect minocycline, which is a tetracycline, to be effective in treating mucositis.

7. Claims 1, 4-6, 12-14, 22-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schenk et al., supra or Rothwell et al, supra in view of Tilg et al., Transplantation, 56 (1), (1993), 196-201. (of record in parent application 09/065,012).

Schenk or Rothwell as applied above.

Schenk or Rothwell do not disclose administering a second therapeutic agent comprising an inflammatory cytokine inhibitor such as TGF-alpha inhibitor, i.e. pentoxifylline; however, the Examiner refers to Tilg et al., which discloses that pentoxifylline is a cytokine inhibitor which is used to treat mucositis in individuals having undergone bone marrow transplantation. Kindly refer to the abstract.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods of Schenk or Rothwell to additionally administer an inflammatory cytokine inhibitor such as pentoxifylline because Rothwell, Schenk and Tilg establish that

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tetracycline and pentoxifylline are known in the art to be useful for treating or preventing mucositis in individuals undergoing treatment for cancer. Modification to combine tetracycline and pentoxifylline, all known to be useful for the same purpose, would have been obvious to one of ordinary skill in the art in view of the fact that the courts have held that “it is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be used for the very same purpose” Kindly refer to In re Susi, 169 USPQ 423, 426 (CCPA 1971). Furthermore, combination of tetracycline and pentoxifylline into a pharmaceutical composition would have been motivated by the reasoned expectation of producing a composition having a synergistic effects.

Concerning claims 23 and 25, in view of the desirable results obtained by Rothwell, it would have been obvious to one of ordinary skill in the art to begin treating the patients a day before radiation or to treat patients undergoing chemotherapy because one of ordinary skill in the art would reasonably expect that such treatment would be equally effective in ameliorating the onset of mucositis.

8. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Rothwell or Schenk in view of Tilg as applied to claims 1, 4-6, 12-14, 22-27 above, and further in view of Stogniew et al., supra.
Rothwell, Schenk and Tilg as applied above.

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Rothwell, Schenk and Tilg do not disclose treating mucositis with minocycline; yet the Examiner refers to Stogniew et al., which discloses methods for treating mucosal tissue damage (mucositis) associated with radiation and/or chemotherapeutic treatment of cancers, the method comprising administering amifostine as well as additional compounds, such as minocycline. Please see the abstract; col. 9, lines 42-56, especially line 56.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods of Schenk, Rothwell and Tilg to administer minocycline as the tetracycline because Stogniew suggest that minocycline may be useful in the treatment of mucositis and one of ordinary skill in the art would reasonably expect minocycline, which is a tetracycline, to be effective in treating mucositis.

9. Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Rothwell or Schenk in view of Tilg as applied to claims 1, 4-6, 12-14, 22-27 above, and further in view of Bondi et al. (of record in parent application 09/065,012).

Rothwell or Schenk and Tilg do not disclose treating mucositis by additionally administering antimicrobial compounds.

Yet, the Examiner refers to Bondi et al., which discloses methods of treating oral mucositis in children undergoing chemotherapy by administering antimicrobial compounds such as tobramycin, polymyxin and amphotericin. Please refer to the abstract.

It would have been obvious to one of ordinary skill in the art to modify the therapeutic methods of Rothwell, Tilg and Schenk to combine administration with the antimicrobial agents

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of Bondi for the treatment of mucositis because the prior art establishes that tetracycline, pentoxifylline and antimicrobials are known in the art to be useful for treating or preventing mucositis in individuals undergoing treatment for cancer. Modification to combine tetracycline, pentoxifylline and antimicrobial compounds, all known to be useful for the same purpose, would have been obvious to one of ordinary skill in the art in view of the fact that the courts have held that "it is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be used for the very same purpose" Kindly refer to In re Susi, 169 USPQ 423, 426 (CCPA 1971). Furthermore, combination of tetracycline and pentoxifylline with the antimicrobial compounds of Bondi into a pharmaceutical composition would have been motivated by the reasoned expectation of producing a composition having a synergistic effect

Double Patenting

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

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11. Claims 15, 19, 20 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 36, 37, 40, 41, 43 of copending Application No. 09/265,299 . Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant application and ‘299 claim a method for treating or preventing mucositis comprising administering an effective amount of tetracycline. The claims of the instant application differ from those of ‘299 because the claims of ‘299 recite “consisting essentially of” language as opposed to the claims of the instant application which recite “comprising” language. Moreover, the claims of the instant application are not limited to the administration of tetracycline only and the claims of the instant application broadly recite the administration of MMP inhibitors.

However, the scope of the claims of the instant application and those of ‘299 overlap because the claims of the instant application are broader and encompass the more specific method of ‘299. Furthermore, at least one of the agents being administered, i.e. tetracycline, is identical.

12. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Claims 1, 4-7, 12-15, 19-27 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cybille Delacroix-Muirheid whose telephone number is (703)

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306-3227. The examiner can normally be reached on Tue-Fri from 8:30 to 6:00. The examiner can also be reached on alternate Mondays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (703) 308-4725. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

CDM

Feb. 10, 2002

Cybille Delacroix
Cydille Delacroix-Muirheid
Patent Examiner Group 1600